

**Serial No.:** 09/132,156  
**Filing Date:** 11 August 1998

Please enter the amendments below and consider the remarks that follow.

IN THE CLAIMS:

Please cancel Claims 30-45, 57 and 58 without prejudice, admission or disclaimer.

Please enter the following new claims:

--59. A method of subjecting a sample to rapid thermal cycling, said method comprising:

a) contacting a sample holder containing a sample with heated fluid, thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time;

b) contacting the sample holder with non-heated fluid, thereby lowering the temperature of the sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time;

c) contacting the sample holder with heated fluid, thereby raising the temperature of the sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time;

wherein steps a) through c) are completed in about 30-60 seconds.

60. The method of Claim 59, wherein steps a) through c) are repeated.

61. The method of Claim 59 or 60, wherein said sample holder is one of a plurality of sample holders.

62. The method of Claim 59 or 60, wherein the first predetermined period of time is about 8 seconds or less.

63. The method of Claim 62, wherein the first predetermined period of time is less than 1 second.

64. The method of Claim 59 or 60, wherein said lowering in step b) occurs in about 25 seconds or less.

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65. The method of Claim 59 or 60, wherein said lowering in step b) occurs at a rate of at least about 1.5 °C per second.

66. The method of Claim ~~59~~ or 60, wherein said lowering in step b) occurs at a rate of up to about 4.1 °C per second.

67. The method of Claim 59 or 60, wherein the difference between said first and said second temperature is up to about 42 °C.

68. The method of Claim 59 or 60, wherein the second predetermined period of time is about 5 seconds or less.

69. The method of Claim 68, wherein the second predetermined period of time is less than 1 second.

70. A method of amplifying a nucleic acid, said method comprising:

a) contacting a sample holder containing a sample comprising a nucleic acid and amplification primer with heated fluid, thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time to denature said double-stranded nucleic acid;

b) contacting the sample holder with non-heated fluid, thereby lowering the temperature of the nucleic acid sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time to anneal said amplification primer;

c) contacting the sample holder with heated fluid, thereby raising the temperature of the nucleic acid sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time to allow amplification of said nucleic acid; and

d) repeating steps a) through c), wherein steps a) through c) are completed in about 30-60 seconds.

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71. The method of Claim 70, wherein said sample further comprises a nucleic acid polymerizing enzyme.

72. The method of Claim 70, wherein said sample holder is one of a plurality of sample holders.

73. The method of Claim 70, wherein the first predetermined period of time is less than 1 second.

74. The method of Claim 70, wherein said lowering in step b) occurs in about 25 seconds or less.

75. The method of Claim 74, wherein said lowering in step b) occurs in about 9 seconds.

76. The method of Claim 70, wherein said lowering in step b) occurs at a rate of at least about 1.5 °C per second.

77. The method of Claim 70, wherein said lowering in step b) occurs at a rate of up to about 4.1 °C per second.

78. The method of Claim 70, wherein the difference between said first and said second temperature is up to about 42 °C.

79. The method of Claim 70, wherein the second predetermined period of time is about 5 seconds or less.

80. The method of Claim 79, wherein the second predetermined period of time is less than 1 second.

81. A method of subjecting a sample to rapid thermal cycling, said method comprising:

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a) raising the temperature of a sample to a first temperature and holding the sample at about said first temperature for a first predetermined period of time;

b) lowering the temperature of the sample to a second temperature at a rate at least about 1.5 °C per second and holding the sample at about said second temperature for a second predetermined period of time.

82. The method of Claim 81, further comprising;

c) raising the temperature of the sample to a third temperature intermediate to said first and second temperatures and holding the sample at about said third temperature for a third predetermined period of time.

83. The method of Claim 81 or 82, wherein the steps are repeated.

84. The method of Claim 81 or 82, wherein said lowering in step b) is at a rate of up to about 4.1 °C per second.

85. The method of Claim 81 or 82, wherein the difference between said first and said second temperature is up to about 42 °C.

86. The method of Claim 81 or 82, wherein the first predetermined period of time is about 64 seconds or less.

87. The method of Claim 81 or 82, wherein the first predetermined period of time is less than 1 second.

88. The method of Claim 81 or 82, wherein the second predetermined period of time is about 80 seconds or less.

89. The method of Claim 81 or 82, wherein the second predetermined period of time is less than 1 second.--.